



US006100541A

United States Patent [19]

[11] Patent Number: **6,100,541**

Nagle et al.

[45] Date of Patent: **Aug. 8, 2000**

[54] MICROFLUIDIC DEVICES AND SYSTEMS INCORPORATING INTEGRATED OPTICAL ELEMENTS

OTHER PUBLICATIONS

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Dasgupta, P.K. et al., "Electroosmosis: A Reliable fluid Propulsion System for Flow Injection Analysis," *Anal. Chem.* 66:1792-1798 (1994), (Month Unknown).

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Jacobson, S.C. et al., "Fused Quartz Substrates for Microchip Electrophoresis," *Anal. Chem.* 67:2059-2063 (1995), (Month Unknown).

[21] Appl. No.: **09/030,535**

Manz, A. et al., "Electrophoresis pumpgin and electrophoretic separations for miniaturized chemical analysis systems," *J. Micromech. Microeng.* 4:257-265 (1994), (Month Unknown).

[22] Filed: **Feb. 24, 1998**

Nussbaum, Ph. et al., "Design, fabrication and testing of microlens arrays for sensors and microsystems," *Pure Appl. Opt.* 6:617-636 (1997), (Month Unknown).

[51] Int. Cl.⁷ **G01N 15/06**

[52] U.S. Cl. **250/573; 250/216; 356/246; 422/9; 204/603**

Ramsey, J.M. et al., "Microfabricated chemical measurment systems," *Nature Med.* 1:1093-1096 (1995), (Month Unknown).

[58] Field of Search 250/573, 216; 356/244, 246; 422/99, 104, 108, 100; 204/601, 297 R, 612, 603

Seiler, K. et al., "Planar Glass Chips for Capillary Electrophoresis: Repetitive Sample Injection, Quantitation, and Separation Efficiency," *Anal. Chem.* 65:1481-1488 (1993), (Month Unknown).

[56] References Cited

U.S. PATENT DOCUMENTS

3,641,354	2/1972	De Ment	250/216
4,390,403	6/1983	Batchelder .	
4,816,695	3/1989	Lavin	250/573
4,908,112	3/1990	Pace .	
5,126,022	6/1992	Soane et al. .	
5,228,969	7/1993	Hernandez .	
5,498,392	3/1996	Wilding et al. .	
5,571,410	11/1996	Swedberg et al. .	
5,585,069	12/1996	Zanzucchi et al. .	
5,593,838	1/1997	Zanzucchi et al. .	
5,603,351	2/1997	Cherukuri et al. .	
5,635,358	6/1997	Wilding et al. .	
5,637,469	6/1997	Wilding et al. .	
5,867,266	2/1999	Craighead	356/344
5,876,675	3/1999	Kennedy	422/99

Seiler, K. et al., "Electrophoresis Pumping and Valveless Control of Fluid Flow within a Manifold of Capillaries on a Glass Chip," *Anal. Chem.* 66:3485-3491 (1994), (Month Unknown).

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FOREIGN PATENT DOCUMENTS

WO 96/04547	2/1996	WIPO .
WO 97/02357	1/1997	WIPO .

[57] ABSTRACT

The present invention provides microfluidic devices and systems that utilize optical detection systems, and where one or more light altering optical elements are integrated into the body structure of the microfluidic device. The resulting devices perform at least a portion of the optical manipulations used in the optical detection method employed.

27 Claims, 4 Drawing Sheets

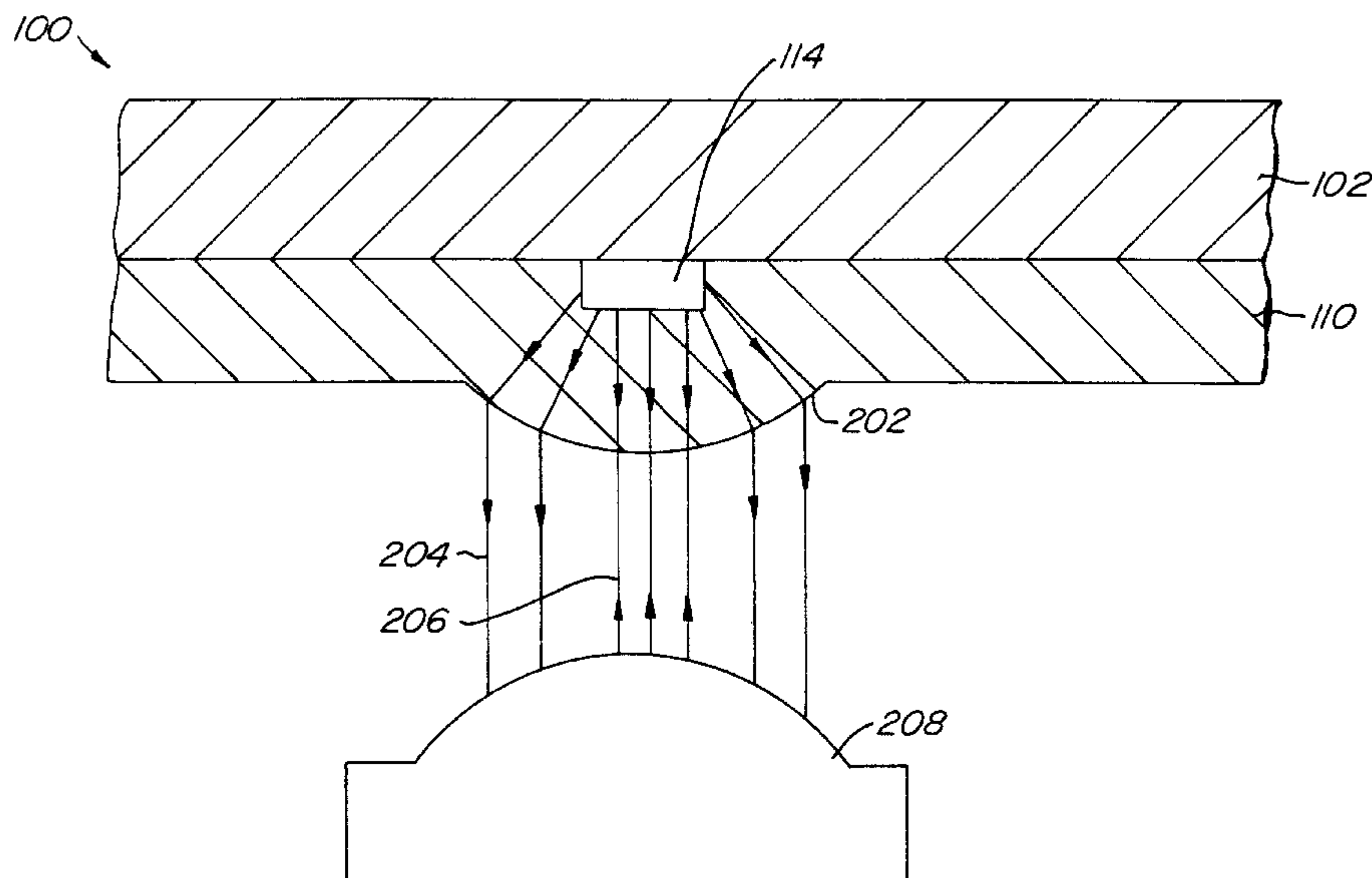
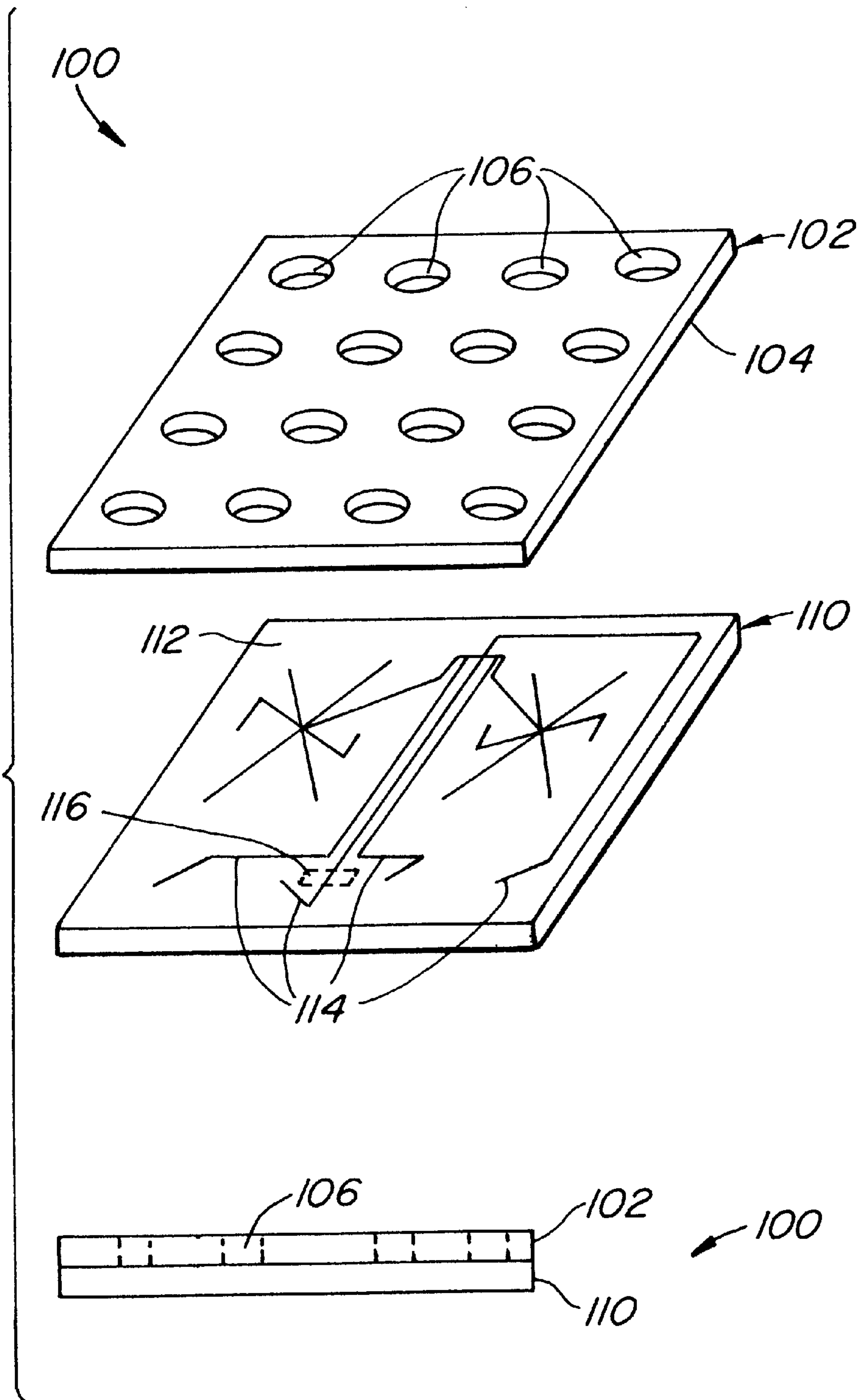


FIG. 1.



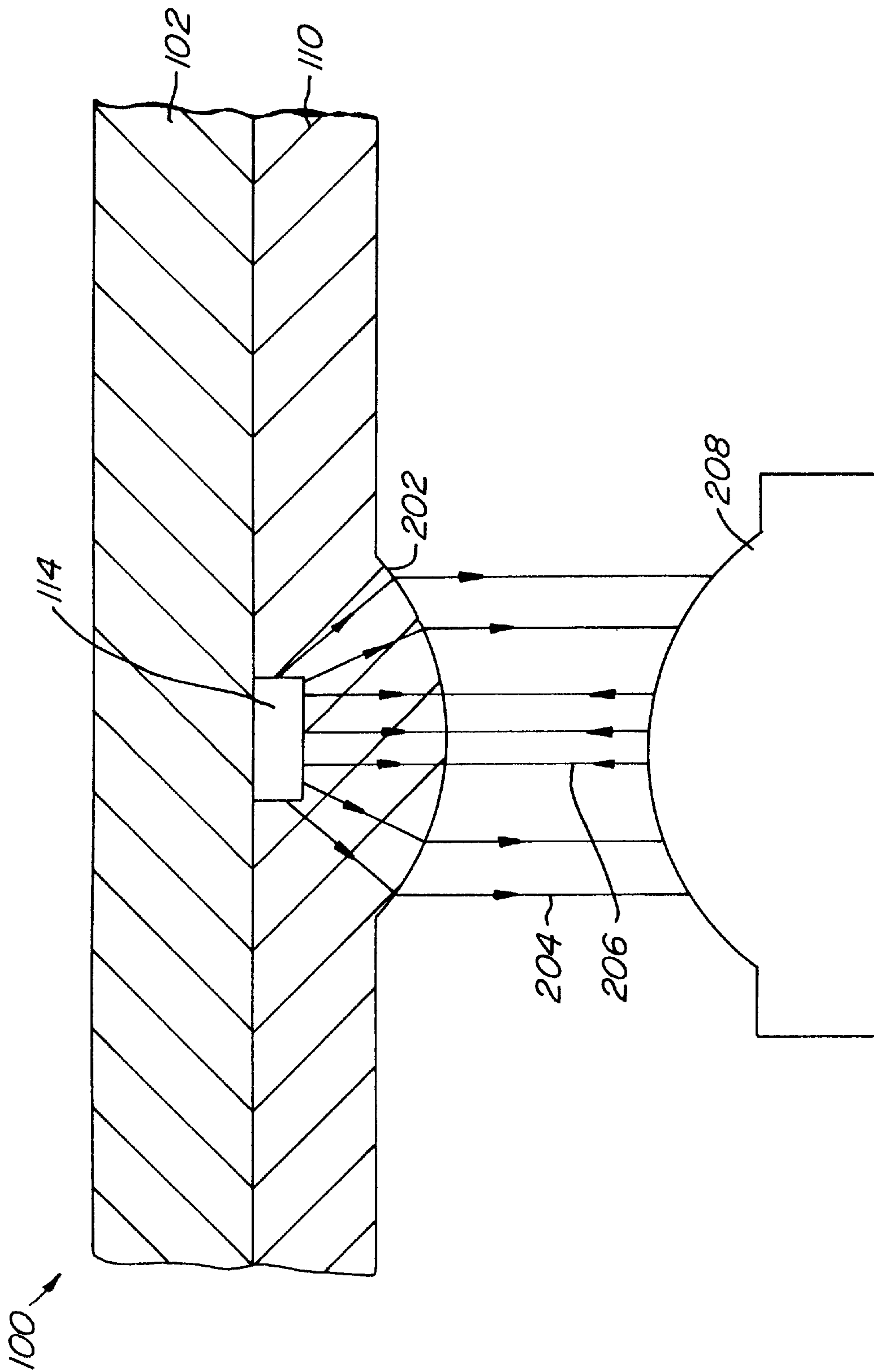


FIG. 2.

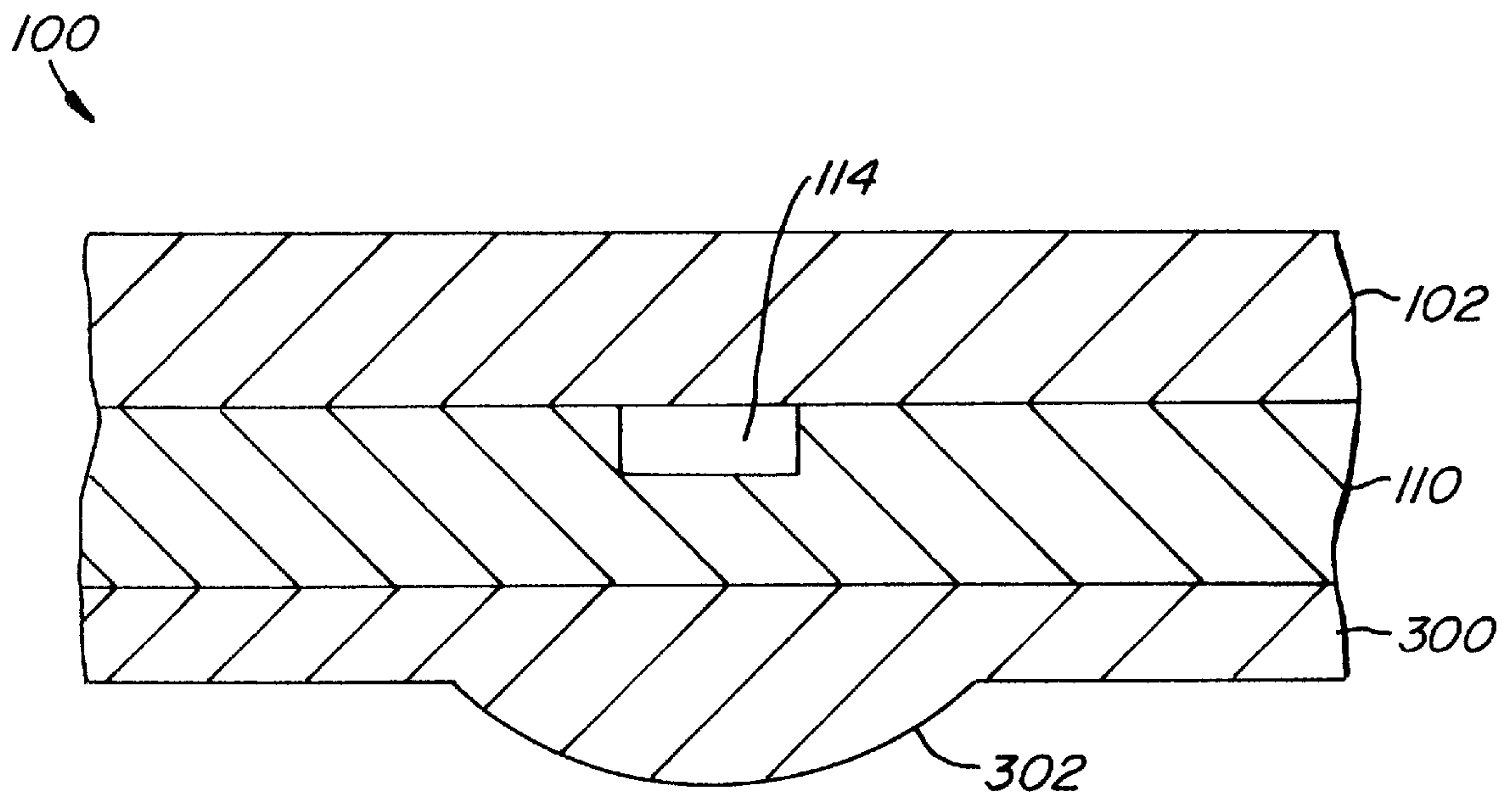


FIG. 3.

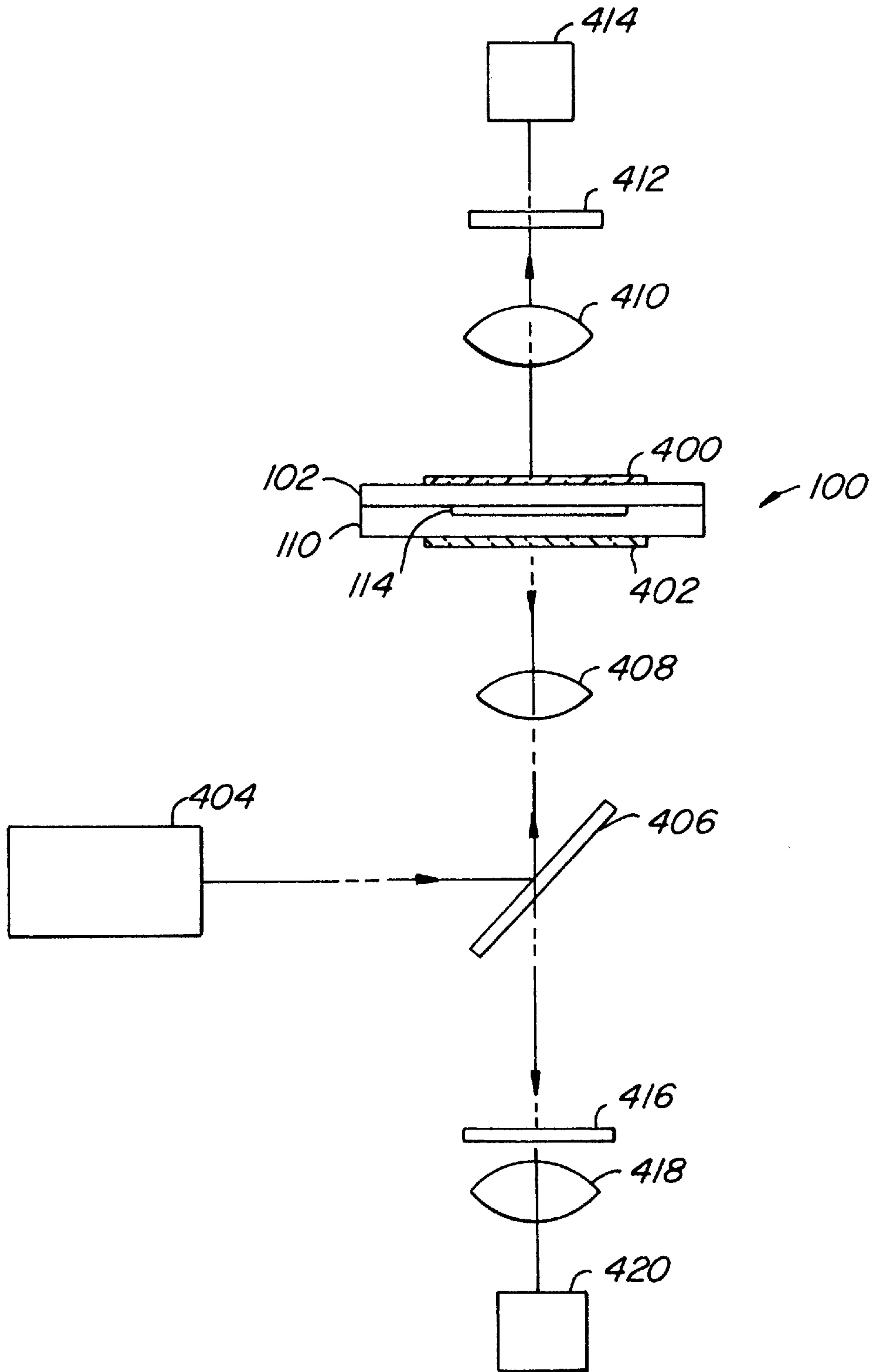


FIG. 4.

MICROFLUIDIC DEVICES AND SYSTEMS INCORPORATING INTEGRATED OPTICAL ELEMENTS

BACKGROUND OF THE INVENTION

The use of microfluidic technology has been proposed for use in a number of analytical chemical and biochemical operations. These technologies provide advantages of being able to perform chemical and biochemical reactions, macromolecular separations, and the like, that range from the simple to the relatively complex, in easily automatable, high-throughput, low-volume systems. In particular, these systems employ networks of integrated microscale channels in which materials are transported, mixed, separated and detected. The small size of these systems allows for the performance reactions at substantially greater rates, and with substantially less reagent volume. Further, the development of sophisticated material transport systems has permitted the development of systems that are readily automatable and highly reproducible.

Because of their small size, microfluidic systems have typically required the use of relatively sophisticated detection systems to monitor the progress and results of the operation being performed by the system. In particular, as noted above, the extreme small scale of some microfluidic systems results in very small volumes of reagents, samples and the like, being used. Consequently, the amount of material that can be ultimately detected, e.g., using an optical detection system, is also very small. In order to address these issues, detection systems have become more sophisticated to either boost the detectable signal produced from material sought to be detected, increase the sensitivity of the instrumentation, or a combination of the two. For example, microscopes equipped with photomultipliers enhance the ability to detect fluorescently labeled materials within microscale channels. Further, the use of laser-induced fluorescence also enhances the amount of signal produced from these fluorescent materials.

Although these sophisticated detection systems have addressed many of the problems associated with detection in microscale fluidic channels, a number of problems remain, such as difficulty in optimally aligning these instruments, the cost and sophistication of providing robust optics for such systems and the like. Further, as the number of applications for microfluidic systems increases, it will include a similar increase in the type of optical detection systems to be used. The use of specifically tailored detection systems for each different application will present a likely prohibitive cost barrier. The present invention addresses many of the problems outlined above, as well as others.

SUMMARY OF THE INVENTION

The present invention provides microfluidic devices for use in performing analytical operations that employ optical detection systems. In particular, the present invention provides microfluidic devices, and systems incorporating such devices, which have at least one component of the optical detection system as a part of the microfluidic device.

In a first aspect, the present invention provides a microfluidic device which comprises a body structure having a microscale channel disposed therein. The device includes a light altering optical element integrated into the body structure adjacent to the microscale channel, whereby at least a portion of light passing from or to the microscale channel is transmitted through the light altering optical element. In preferred aspects, the body structure of the device comprises

a first planar substrate having at least first and second opposing planar surfaces, the microscale channel being fabricated into the first planar surface of the first substrate, and the light altering optical element being fabricated into the second planar surface of the first substrate adjacent to the microscale channel in the first planar surface. Also included is a second planar substrate overlaying the first surface of the first planar substrate.

In an alternate aspect, a third substrate layer is provided having at least a first planar surface and a second surface. The first planar surface of the third substrate layer is bonded to one of the second planar surface of the first planar substrate or the second planar surface of the second planar substrate. The third substrate also includes a light altering optical element fabricated into the second surface of the third substrate.

In still another related aspect, the present invention also provides a microfluidic device, which comprises a body structure having an interior portion and an exterior portion. At least a first microscale channel is disposed within the interior portion of the body structure. A detection window is provided disposed on the exterior portion of the body structure, whereby the detection window provides optical access to the at least one microscale channel. In this aspect, the detection window comprises a light altering optical element integrated into the body structure.

Also provided by the present invention are microfluidic systems, which comprise a microfluidic device comprising a body structure, at least a first microscale channel disposed in the body structure, a transparent region in the body structure, the transparent region including a light altering optical element integrated into the body structure. The systems of the invention also typically comprise an optical detector disposed adjacent to the detection window. The optical detector comprises an objective lens for collecting an optical signal transmitted from the microscale channel via the light altering optical element, and a light detector for measuring an amount of light collected.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 schematically illustrates a general microfluidic device having a body structure that incorporates multiple substrate layers.

FIG. 2 is a schematic illustration from a side view of a microfluidic device having a light altering optical element integrated into the body structure of the device.

FIG. 3 is a schematic illustration of an alternative device, having a light altering optical element integrated into the body structure of the device through the incorporation of an additional substrate layer that includes the optical element.

FIG. 4 is a schematic illustration of a system utilizing a microfluidic device that includes polarizers integrated into the overall body structure of the device, and a detector system for use with such device.

DETAILED DESCRIPTION OF THE INVENTION

I. General

The present invention generally provides microfluidic devices that have one or more optical elements that are employed in the use of such devices, as an integral portion of the device itself, e.g., incorporated into or attached to the body structure of the device. These devices address a number of the problems that are associated with optical detection systems that have been used in conjunction with microfluidic systems.

Typical microfluidic systems employ a body structure or substrate that has at least one microscale channel disposed within it. Examples of such systems range from simple tubular capillary systems, e.g., fused silica capillaries, to more complex planar devices that can have from one to several intersecting channels disposed therein, i.e., between at least two planar substrate layers. Microfluidic systems generally have a broad range of uses including separation and characterization of macromolecular species, e.g., proteins and nucleic acids, see e.g., U.S. Pat. No. 5,699,157, screening assay platforms, e.g., drug screening, diagnostics, etc. See, e.g., commonly owned Published PCT Application No. WO 98/00231, each of which is incorporated herein by reference in its entirety for all purposes.

In many cases, microfluidic systems utilize optical detection systems in the performance of their analytical and/or synthetic functions. These optical detection systems generally require the presence within the microfluidic system of an optical access point, e.g., a detection window, whereby light energy can be transmitted to and from one or more channels of the system. Such detection windows are typically made up of at least a transparent region of the body structure of the device. This is a simple solution where body structures are fabricated from transparent substrates, e.g., glass, quartz or transparent polymers.

In operation, an optical detector is placed adjacent the transparent region of the device, where it collects optical signals from the channels of the device. The optical detector, for its part, typically includes a number of optical elements to aid in the reception, transmission and detection of the optical signal. Many of these optical elements are capable of affecting or altering the light that passes through them. As used herein, a "light altering" capability, is the ability of an optical element to alter the amount, spectrum, direction, path, or polarity of light passing through that optical element. Some examples of such light altering elements include lenses, optical gratings, filters, beam splitters, mirrors, optical coatings, e.g., antireflective coatings, and the like. Optical detectors also often include light sources, i.e., lasers, LEDs, high intensity lamps, etc., for directing light at the channel for, e.g., fluorescent, absorbance-based or colorimetric detection schemes.

While the optical detection systems described above have proven very useful in the operation of microfluidic systems, these detection systems have a number of drawbacks. For example, because microfluidic systems utilize extremely small-scale channels in which detection occurs, alignment of an external detector at the detection point becomes a difficult proposition. In particular, one must align an external detector with precision in order to capture optimal signal from channels that typically range from about 10 to about 100 μm wide. Alignment of the detection optics is generally carried out by scanning the detector across the detection window, e.g., in the x-y axes, until an optimal signal indicative of alignment is achieved. This type of alignment, however, is very time consuming, and in the case of automatic alignment systems, has an additional cost in terms of the required equipment, and the like. A similar method is employed in focusing these detection systems, where the detector is moved along the z-axis, e.g., closer to and further from the device, until an optimal signal is received.

Similarly, because there is typically an air gap between the substrate or device and the first optical element of the detector, the light delivery and collection efficiencies of such systems are also reduced.

In addition to problems with alignment and light collection efficiency, optical detection systems also must typically

be tailored to the particular application being performed within the microfluidic device. For example, fluorescence based detectors typically must include high intensity light sources, dichroic filters, beam splitters, photomultipliers and the like, to excite fluorescent species in the channel, separate the emitted fluorescence from the reflected excitation light, and measure the emitted fluorescence. Additionally, the combination of different filters, dichroics and beam splitters must be tailored further for the specific fluorescent spectra of the operation that is being performed within the system, e.g., depending upon the fluorescent label, or combination of fluorescent labels used. Different detection schemes, e.g., absorbance, i.e., U.V. or colorimetric, require a different set of optical elements, by virtue of having little or no need for light-separation optics. The need for optical systems that are specifically tailored for different detection schemes, assays or the like, further escalates the costs associated with performing the full range of optical analyses in microfluidic systems.

In accordance with the present invention, microfluidic devices are provided where the body structure is fabricated to include at least one light altering optical element. The incorporation of such elements into the body structure of the device permits the use of more universal detection systems, as the microfluidic device itself meets many of the specific optical requirements for its particular application. Additionally, incorporation of optical elements also can facilitate alignment of microfluidic devices within the detection system, by providing a pre-aligned lens. Further, the inclusion of integrated optical elements provides enhanced efficiencies in terms of light collection and delivery. For example, incorporation of a lens molded into the body structure or substrate of the device allows for a numerical aperture (NA) that can be greater than 1, and light delivery and collection efficiencies for lenses are both proportional to $(\text{NA})^2$. Similarly, losses due to total internal reflection are minimized.

In a further advantage, the incorporation of certain optical elements in the mass produced microfluidic devices can provide advantages in terms of cost, over the inclusion of more robust versions of the same elements in the detection instrumentation.

II. Integrated Optical Components

As noted above, the microfluidic devices of the present invention typically comprise a body structure having one or more microscale channels disposed therein. As used herein, the term "microscale or microfluidic channel" refers to a fluid channel or conduit that has at least one cross-sectional dimension, e.g., width, depth or diameter, of between about 0.1 and 500 μm . Preferably, such channels have at least one cross sectional dimension in the range of from about 1 to about 200 μm and more preferably, from about 5 to about 100 μm .

In preferred aspects the microfluidic devices described herein are planar in structure, although non-planar device structures, e.g., tubular structures, are also possible within the scope of the present invention. In the planar device structures, the body portion of the device is typically fabricated from one or more planar substrate layers. An example of this planar layered structure is illustrated in FIG. 1. In particular, the body of the microfluidic device **100** includes a first planar substrate **110** that is fabricated with a series of grooves and/or depressions **114** in its upper surface **112**. These grooves or depressions correspond to the channel/chamber geometry of the finished device. A second planar substrate **102** is then overlaid and its lower surface **104** is bonded to the surface of the first substrate to seal and

define the last wall of the channels/chambers of the device. Optional ports/reservoirs **106** are provided in the body structure and in fluid communication with the channels of the device, to provide fluid and/or electrical access to the channels. These ports/reservoirs are generally provided as apertures disposed through the upper substrate layer **102**, e.g., connecting the upper surface with lower surface **104**, whereby they will fluidly communicate with one or more of the sealed channels **114**. These devices also typically include an optical detection window **116** to permit measurement of optical signals from the channels. Examples of microfluidic devices incorporating this planar body structure are described in substantial detail in Published PCT Application No. WO 98/00231, WO 98/00705, and U.S. patent application Ser. No. 08/845,754, filed Apr. 25, 1997, now U.S. Pat. No. 5,976,336, each of which is incorporated herein by reference.

Typically, these microfluidic devices employ fluid or material direction systems to transport fluids or other materials through and among the channels and chambers of the device in order to perform the combinations, separations or other operations in carrying out a given analysis. Examples of such transport systems include pneumatically or hydraulically driven systems, e.g., as described in published PCT Application No. 97/02357, systems incorporating microfabricated pumps and/or valves, and, in preferred aspects, electrokinetic material transport systems, e.g., as described in Published PCT Application No. 96/04547.

As noted above, the microfluidic devices of the present invention include an optical detection window disposed in the body structure of the device adjacent to one or more of the included microscale channels. In accordance with the present invention, these optical detection windows include at least one light altering optical element integrated into the body structure of the device. As used herein, the phrase "integrated into" refers to optical elements that are either fabricated into the body structure or are attached to the body structure such that the optical element(s) and body structure form(s) a single integrated unit. The light altering optical element is capable of transmitting light while altering the amount, spectrum, polarity or path of the light transmitted therethrough. The integrated optical element may be fabricated into, or attached to the body structure, as described in greater detail below. Examples of particularly preferred optical elements include lenses (e.g., spherical, aspheric, fresnel, binary) to perform magnifying, demagnifying, collimating, light delivery, light collection or focusing functions, optical filters (spatial or wavelength selecting), optical gratings, optical coatings (e.g., dichroic, antireflective, reflective), beam splitters, waveguides, TIR mirrors, polarizers and the like. For a discussion of these optical elements, see, e.g., Handbook of Optics, volume II, (1995 McGraw-Hill), which is incorporated herein by reference in its entirety for all purposes.

In one aspect of the present invention, the optical elements described above are typically fabricated into one of the substrate layers that makes up the body structure of the device, e.g., the first or second substrate layer described previously. A schematic illustration of a device incorporating an optical element in one of the layers of the body structure is shown in FIG. 2. As shown, the device **100** includes a first planar substrate layer **110** and a second planar substrate layer **102**. The channel(s) of the device **114** (shown in cross-section) are fabricated into the first substrate layer **110** as a groove or depression. The second substrate layer **102** is overlaid and bonded to the first substrate **110** to seal the channel(s) **114**. An optical element, shown in FIG. 2 as

collimating lens **202** is also shown fabricated into the first substrate layer **110** at the point of the optical detection window (**116** from FIG. 1). The lens **202** is positioned so as to permit transmission of an optical signal from the channel **204**, as well as permitting transmission of external light energy **206** into the channel, e.g., for use in fluorescence or absorbance based detection. In particular, as shown, lens **204** is illustrated as a collimating lens, whereby light emitted from, or reflected by the contents of the channel **114**, passes through lens **204** and is collimated, so as to be efficiently collected by the optical detection system, as represented by objective lens **208**. As shown, the collimating lens **204** allows more light to be gathered by the objective lens **208**, as well as allows simpler alignment of the objective lens, e.g., over larger lens **204**, as opposed to the much smaller channel **114**.

As illustrated, the optical element is fabricated into the same substrate into which was fabricated the fluidic elements of the device, e.g., the microscale channels. In many cases, this permits the fabrication of both the fluidic and optical elements in the same fabrication step. In particular, where polymeric substrates are used in the body structure of the overall device, the same fabrication techniques used in producing the fluidic elements, e.g., injection molding, embossing, and the like, are also used to fabricate structurally defined optical elements. Although not shown, it will be appreciated that the optical element can also be fabricated into the upper substrate, depending upon the orientation of the optical detector relative to the device, i.e., above or below.

In an alternate aspect, the microfluidic devices of the present invention include an additional substrate layer, i.e., in addition to the at least first and second substrate layers, that incorporates the light altering optical element or elements, but does not necessarily define any of the fluidic elements of the microfluidic device. The additional substrate layer is typically attached to the body structure of the microfluidic device, e.g., by bonding, clamping, or other substantially secure coupling methods.

An example of a microfluidic device incorporating this alternate structure is illustrated in FIG. 3. Again, as shown, the device **100** includes a body structure that is made up of at least two planar substrate layers **102** and **110**. The channels **114** of the device (shown in cross-section), are again fabricated into the surface **112** of substrate **110**. In the aspect illustrated in FIG. 3, a third substrate layer **300** is bonded or attached to the bottom surface of lower substrate **110**. This third substrate layer includes a light altering optical element, shown as lens **302**, fabricated into the third substrate layer **300**. The use of one or more auxiliary layers for the addition of optical elements to the microfluidic device body structure, permits a more generalized manufacturing method for the fluidic structures of the device, e.g., channels, ports and the like. Specifically, a single type of channel and port geometry, e.g., layout, can be used in performing a number of different types of analyses, each requiring somewhat different optics in its detection scheme. As such, each different type of device can be provided with any of a number of different optical elements by simply attaching an appropriate third substrate layer having the appropriate optical element fabricated into it. In this aspect, the present invention provides still a further level of interchangeability, namely, interchangeability of fluidic elements, as well as the interchangeability of the optical detectors. Examples of a cover layers that are readily attached to the body structure of the device are described in commonly owned U.S. patent application Ser. No. 09/028,

965, filed on Feb. 24, 1998 entitled "Microfluidic Devices and Systems Incorporating Functional Cover Layers," filed of even date (Attorney Docket No. 100/03700), which is incorporated herein in its entirety for all purposes. Specifically, the optical elements described herein are readily included in a functional cover layer that is attached to the body structure of the device.

Fabrication of the light altering optical element into the surface of one of the substrate layers of the body structure is generally carried out by any of a number of well known manufacturing techniques, depending upon the type of optical element that is being used. For example, substrate layers incorporating structurally defined optical elements, e.g., lenses, optical gratings, etc., are optionally fabricated from polymeric materials, thus allowing production of the optical element as a portion of the overall fabrication process. Specifically, the polymeric substrates incorporating these optical elements may be produced using, e.g., injection molding, embossing, LIGA and related processes. This is particularly useful where the substrates that make up the microfluidic elements of the device also are fabricated from polymeric materials, so that a single mold can define/provide for both the microfluidic and optical elements of the microfluidic device. In particular, a mold for the planar substrate provides on one surface, features that define the fluid channels of the overall device, and on the opposing surface, features that define the optical element. These polymer fabrication techniques are equally applicable to substrate layers that are used simply to add optical elements to the body structure of the device.

The use of polymeric materials in the fabrication of microfluidic devices is described in detail in U.S. patent application Ser. No. 08/843,212, filed Apr. 14, 1997, now U.S. Pat. No. 5,885,470, and incorporated herein by reference in its entirety for all purposes. Examples of suitable polymeric materials for use in fabrication of the substrate layers of the microfluidic devices described herein include, e.g., polydimethylsiloxanes (PDMS), polymethylmethacrylate (PMMA), polyurethane, polyvinylchloride (PVC), polystyrene, polysulfone, polycarbonate and the like.

In some cases, the microfabrication methods described for use in fabrication of the channel structures in non-polymer substrates are optionally used in fabricating optical elements into the surface of the substrates, e.g., in the case of silica substrates. For example, optical gratings, binary optics or fresnel lenses are optionally etched into the surface of the substrate using the lithographic methods described herein, e.g., photolithography, wet chemical etching, and the like. See Handbook of Optics, vol II pp7.18-7.21 and 8.1-8.18 (McGraw-Hill 1995), previously incorporated herein by reference.

In a number of instances, substrate layers incorporating the light altering optical element are fabricated from, or alternatively, coated with materials that have the desired light altering characteristics. For example, in the case of optical filters, one or more substrate layers in the body structure may be coated with materials that will transmit light falling within a desired wavelength range. Examples of such coatings include standard interference-type filters made form periodic layers of materials with different indices of refraction, and controlled thicknesses.

Polarizers are also optionally included as the light altering element on the body structure of the microfluidic devices described herein. Such polarizers are typically employed where the overall device is used to perform fluorescence polarization detection based assays run in the channels of the device. An example of a device and system that incorporates

integrated polarizers for use in such fluorescent polarization assays is schematically illustrated in FIG. 4.

As shown, the microfluidic device **100**, includes a microfluidic channel **114** disposed between upper and lower substrates **102** and **110**, respectively. Attached to and integrated with the outer surfaces of the device **100**, are polarizers **400** and **402**. The overall system into which the microfluidic device is placed, includes a source of unpolarized excitation light **404**. Excitation light, e.g., having an appropriate excitation wavelength, from source **404** is directed at dichroic mirror **406** which is typically selected to reflect the excitation light while permitting emitted light, e.g., fluorescence, to pass. Excitation light reflected by the dichroic mirror **406** is focused by lens **408** through polarizer **402** and onto channel **114** whereby it activates any fluorescent species therein. Polarizer **402** is typically oriented in a first plane (e.g., parallel with the plane of the figure sheet) while polarizer **400** is oriented in the perpendicular plane (e.g., perpendicular to the figure sheet). Emitted fluorescence that is in the same plane as polarizer **400** passes through that polarizer and is focused via lens **410**, through filter **412**, and is detected by photodetector **414**, which is optionally a photodiode, PMT or the like. Filter **412** is provided to filter out any excitation light that passes through the device **10** and polarizers **400** and **402**. Emitted fluorescence in the same plane as polarizer **402** passes through that polarizer, through lens **408**, and through dichroic **406**. This fluorescence then passes through filter **416**, and is focused via lens **418** onto photodetector **420**.

Antireflective coatings are optionally included on the body structure to prevent the adverse effects of internal reflectance of the body structure. Such coatings are generally well known in the art and include, e.g., silicon dioxide (SiO₂), magnesium fluoride and the like.

Although illustrated in terms of lenses or coatings, a number of light altering optical elements are optionally incorporated, either alone, or in combination with one or more other optical elements. For example, optical gratings are optionally included to spectrally filter or separate light. Similarly, prisms or beam splitters are optionally included to redirect or separate light directed at or transmitted from the channels of the microfluidic device.

In operation, the microfluidic devices of the present invention are generally used as a portion of a larger microfluidic system. As noted above, such systems typically include a material transport system. For example, in the case of hydraulic or pneumatic material transport systems, the device is typically coupled to an appropriate pressure or vacuum source, either for moving materials through the channels, or for operating microfabricated pumps and valves to move the materials through the channels. Alternatively, the device is coupled with an electrical controller, which applies appropriate currents and/or voltages through the channels of the device to affect electrokinetic material transport. Examples of particularly preferred electrical controller systems are described in substantial detail in Published PCT Application No. 98/00707, previously incorporated herein by reference in its entirety for all purposes.

In addition to material transport systems, the microfluidic systems of the present invention also typically include an optical detection system. Optical detection systems used in the overall microfluidic systems of the invention typically include an optical train for directing an optical signal from the microfluidic channels of the device via the optical element integrated therein, to an appropriate light detector, such as a photodiode or photomultiplier tube. In particularly preferred aspects, the detector includes a light source for

directing an appropriate amount of light energy at the channels of the device, in order to produce a measurable optical signal, e.g., fluorescence, absorbance, etc. Examples of appropriate light sources include, e.g., lasers, laser diodes, LEDs, high intensity lamps, and the like. The light energy from the light source is typically directed to the microscale channel of the device via the optical train, as well as the optical element integrated into the device, which are used to transmit the signal back to the detector.

All publications and patent applications referenced herein are hereby incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference. Although the present invention has been described in some detail by way of illustration and example for purposes of clarity and understanding, it will be apparent that certain changes and modifications may be practiced within the scope of the appended claims.

What is claimed is:

1. A microfluidic device comprising a body structure; at least two intersecting microscale channels disposed in the body structure;

a light altering optical element integrated into the body structure adjacent to a first one of the at least two intersecting microscale channels, whereby at least a portion of light passing from or to the first microscale channel is transmitted through the light altering optical element.

2. The microfluidic device of claim **1**, wherein the light altering optical element is selected from the group consisting of a lens, an optical grating, a wavelength selective filter, a spatial optical filter, a prism, a polarizer and an optical coating.

3. The microfluidic device of claim **2**, wherein the light altering optical element comprises a lens.

4. The microfluidic device of claim **3**, wherein the lens is selected from the group consisting of a magnifying lens, a demagnifying lens, and a collimating lens.

5. The microfluidic device of claim **2**, wherein the light altering optical element comprises a wavelength selective filter.

6. The microfluidic device of claim **1**, wherein the body structure comprises:

a first planar substrate having at least first and second opposing planar surfaces, the at least two intersecting microscale channels being fabricated into the first planar surface of the first substrate, and the light altering optical element being fabricated into the second planar surface of the first substrate adjacent to the microscale channel in the first planar surface; and

a second planar substrate overlaying the first surface of the first planar substrate.

7. The microfluidic device of claim **6**, wherein the first and second substrate layers comprise a polymeric material.

8. The microfluidic device of claim **7**, wherein the polymeric material is selected from the group consisting of polydimethylsiloxane (PDMS), polymethylmethacrylate (PMMA), polyurethane, polyvinylchloride (PVC), polystyrene, polysulfone, and polycarbonate.

9. The microfluidic device of claim **2**, wherein the light altering optical element comprises a light altering optical coating disposed on an outer surface of the body structure.

10. The microfluidic device of claim **1**, wherein the body structure comprises:

a first planar substrate having at least first and second opposing planar surfaces, the at least two intersecting microscale channels being fabricated into the first planar surface of the first substrate;

a second planar substrate having at least a first planar substrate, said first planar substrate being bonded to the first planar surface of the first substrate;

a third substrate layer having at least a first planar surface and a second surface, the first planar surface being attached to one of the second planar surface of the first planar substrate or the second planar surface of the second planar substrate, and wherein the light altering optical element is fabricated into the second surface of the third substrate and positioned to receive and transmit light energy to and from the first microscale channel.

11. The microfluidic device of claim **10**, wherein at least the third substrate layer comprises a polymeric material.

12. The microfluidic device of claim **11**, wherein the polymeric material is selected from the group consisting of polydimethylsiloxane (PDMS), polymethylmethacrylate (PMMA), polyurethane, polyvinylchloride (PVC), polystyrene, polysulfone, and polycarbonate.

13. A microfluidic device, comprising:

a body structure having an interior portion and an exterior portion;

at least two intersecting microscale channels disposed within the interior portion of the body structure;

a detection window disposed on the exterior portion of the body structure, the detection window providing optical access to a first one of the at least two microscale channels, the detection window comprising a light altering optical element integrated with the body structure.

14. A microfluidic system comprising:

a microfluidic device comprising a body structure, at least two intersecting microscale channels disposed in the body structure, a transparent region in the body structure, the transparent region including a light altering optical element integrated into the body structure; an optical detector disposed adjacent to the detection window, the optical detector comprising an objective lens for collecting an optical signal transmitted from a first one of the at least two intersecting microscale channels via the light altering optical element, and a light detector for measuring an amount of light collected.

15. The microfluidic system of claim **14**, wherein the light detector includes one of a photomultiplier tube and a photodiode.

16. The microfluidic system of claim **14**, wherein the optical detector further comprises a processor operably linked to the light detector, for recording an amount of light detected by the light detector.

17. The microfluidic system of claim **14**, further comprising an electrokinetic material transport system, the electrokinetic material transport system comprising:

a plurality of electrodes in electrical contact with different points in the microscale channels; and

an electrical power supply separately electrically coupled to each of the plurality of electrodes for delivering a separate voltage to each of the plurality of electrodes to create a voltage gradient between the different points on the microscale channel.

18. A microfluidic device comprising

a body structure;

a microscale channel disposed in the body structure;

a light altering optical coating disposed on the body structure adjacent to the microscale channel, whereby

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at least a portion of light passing from or to the microscale channel is transmitted through the light altering optical coating.

19. The microfluidic device of claim 18, wherein the light altering optical coating is selected from the group consisting of a wavelength selective filter, a spatial optical filter, and an antireflective coating.

20. The microfluidic device of claim 18, wherein the light altering optical coating comprises one of a silicon dioxide layer and a magnesium fluoride layer.

21. The microfluidic device of claim 18, wherein the body structure comprises:

a first planar substrate having at least first and second opposing planar surfaces, the microscale channel being fabricated into the first planar surface of the first substrate, and wherein the light altering optical coating is disposed on the second planar surface of the first substrate adjacent to the microscale channel in the first planar surface; and

a second planar substrate overlaying the first surface of the first planar substrate.

22. The microfluidic device of claim 21, wherein the first and second substrate layers comprise a polymeric material.

23. The microfluidic device of claim 22, wherein the polymeric material is selected from the group consisting of polydimethylsiloxane (PDMS), polymethylmethacrylate (PMMA), polyurethane, polyvinylchloride (PVC), polystyrene, polysulfone, and polycarbonate.

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24. The microfluidic device of claim 18, wherein the light altering optical coating is disposed on an outer surface of the body structure.

25. The microfluidic device of claim 18, wherein the body structure comprises:

a first planar substrate having at least first and second opposing planar surfaces, the microscale channel being fabricated into the first planar surface of the first substrate;

a second planar substrate having at least a first planar substrate, said first planar substrate being bonded to the first planar surface of the first substrate;

a third substrate layer having at least a first planar surface and a second surface, the first planar surface being attached to one of the second planar surface of the first planar substrate or the second planar surface of the second planar substrate, and wherein the light altering optical coating is disposed on the second surface of the third substrate and positioned to receive and transmit light energy to and from the microscale channel.

26. The microfluidic device of claim 25, wherein at least the third substrate layer comprises a polymeric material.

27. The microfluidic device of claim 26, wherein the polymeric material is selected from the group consisting of polydimethylsiloxane (PDMS), polymethylmethacrylate (PMMA), polyurethane, polyvinylchloride (PVC), polystyrene, polysulfone, and polycarbonate.

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